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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HARLE, JENNIFER I

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
02/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,441	LI ET AL.	
	Examiner	Art Unit	
	Jennifer I. Harle	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72,74-79,81-83,85,92,96-99,101-103,105,107,113-116,119 and 120* is/are pending in the application.

4a) Of the above claim(s) *76-79,119 and 120* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72,74,75,81-83,85,92,96-99,101-103,105,107 and 113-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/20/05; 11/28/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 72-120 were pending and subject to an Election/Restriction requirement. Applicants cancelled claims 73, 80, 84, 86-91, 93-95, 100, 104, 106, 108-112, 117, and 118, and withdrew claims 119-120, in the Amendment and Response to Restriction Requirement, filed November 28, 2007. Applicants elected Group I, claims 72-118, with an election of species to BMP-2, biphosphonate – specifically alendronate, 100% hyaluronic acid esters, Hyaff11p65, and organic solvent.

Election/Restrictions

2. Applicant's election of Group I, claims 72-118, with an election of species to BMP-2, biphosphonate – specifically alendronate, 100% hyaluronic acid esters, Hyaff11p65, and organic solvent, in the reply filed on November 28, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicants notes that water is a species of the genus aqueous buffer and organic solvent is also a genus. Applicants election of the genus of organic solvents rather than a species such as ethanol is noted. In the interest of expediting prosecution but without waiving any part of the restriction requirement, the examiner will examine organic solvents.

3. Claims 76-79 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 28, 2007.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 113-115 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are directed to extruding the osteogenic mixture in an nonsolvent, where the examples of the nonsolvent are water and ethanol. However claim 105 clearly recites wherein the hyaluronic acid ester is prepared by hydration or solubilization of … hyaluronic benzyl esters in water, an organic solvent or an aqueous buffer and Applicants argue in their response to the restriction requirement that water is a species of aqueous buffers. Thus, we have water claimed as a solvent, i.e. hydration or solubilization, which forms a paste or a gel and also a non-solvent. Additionally, ethanol is a common organic solvent. See, e.g. Common Organic Solvents: Table of Properties, 2007, pp. 1-3, http://www.organicdivision.org/organic_solvents.html, printed January 31, 2008. Water and ethanol can't be both solvents and non-solvents.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 72, 74-75, 85, and 92 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim, et al., (WO 01/28602 A1) (provided by the Applicants).

Kim discloses an injectable, including intraosseous injections, formulation comprising a pharmaceutically acceptable admixture of an osteogenic protein, hyaluronic acid derivatives and tricalcium phosphate and formulating porous injectable gels and pastes. Abstract, pg. 1, lines 4-8, pg. 2, lines 13-15, pg. 3, lines 7-9. Kim additionally discloses that the injectable formulation of the invention allows for closed fracture repair and other skeletal tissue without an open reduction procedure as is necessary with implantable devices and that the methods for preparing injectable gels or pastes useful as a carrier for osteogenic protein are made by transforming various non-woven pads and sponges of hyaluronic acid benzyl ester into injectable gel or paste formulations by hydration or solvent addition yielding gels with in vivo residence times from days to up to several months, which can be used to promote the formation of cartilage and/or bone, for repair of tissue damage and fractures, cartilage and/or bone repair and/or growth, Pg. 2, lines 15-27, pg. 3, lines 7-12. Kim further discloses that the preferred osteogenic proteins for use are those of the BMP class identified as BMP-1 through BMP-12, with the most preferred being BMP-2. Kim states that injectable formulations may also find application to other bone sites such as bone cysts, bone defects, intraosseous sites and closed fractures, and that formulations may be used as a substitute for autologous bone graft in fresh and non-union fractures; spinal fusions; bone defect repair in the orthopaedic field; cranio/maxillofacial reconstructions; prosthesis integration, especially as a surface coating to improve fixation of prosthetic implants; in osteomyelitis for bone regeneration; in the dental field for augmentation

of the alveolar ridge and periodontal defects and tooth extraction sockets; in the treatment and/or prevention of osteoporosis, or the treatment of osteoporotice or osteopenic bone. Kim then discusses the addition of other components to the osteogenic protein/hyaluronic acid benzyl ester composition based upon conditions to be treated, i.e. with osteomyelitis antibiotics may be added and other drugs, growth factors, peptides, proteins, cytokines, oligonucleotides, antisense oligonucleotides, DNA and polymers may be added. Pp. 4-5, lines 16-25. Kim then discloses the preparation of injectable hyaluronic acid esters using Hyaff11, Hyaff11p80 and Hyaff11p65 using organic solvents (Hyaff11 and Hyaff11p80) and aqueous buffers (Hyaff11p65) to which rhBMP-2 was added. Pp. 6-7. The in vitro release kinetics, rat ectopic assay, and in vivo biodistribution were evaluated. Pp. 6-11. The examiner notes that although the reference does not specifically indicate that the composition is in the form of a solid rod, it would implicitly be so, because when pastes/gels are injected through a needle for intraosseous injections, or otherwise, the material coming out of the needle is in the form of a solid rod because it is being extruded, in a similar fashion to the instant application's extrusion from a needle.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 72, 74-75, 85, and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim, et al., (WO 01/28602 A1) (provided by Applicants).

Kim teaches as set forth above. Kim does not explicitly teach that the composition is in the form of a cylindrical rod. Although the reference does not specifically indicate the device is in the form of a solid rod, it is obvious to one of ordinary skill in the art that the device, which is injected intraosseously as a paste/gel is in a form of a solid rod because it is made in essentially the same way, i.e. hydrating the Hyaff11p65, where the buffer contains the rhBMP-2, and extruded from the needle and would have the shape of the needle, i.e. a cylindrical rod.

11. Claims 72, 73-74, 85, 92, 97, 98, 99, 105, 107, and 113-116 rejected under 35 U.S.C. 103(a) as being unpatentable over Kim, et al., (WO 01/28602 A1) (provided by Applicants) in view of Vercruysee, et al., Hyaluronate Derivatives in Drug Delivery, Critical Review in Therapeutic Drug Carrier Systems, 1998, 15(5), 513-555 and Campoccia, et al., Semisytnetic resorbable materials from hyaluronan esterification, Biomaterials, 1998, 19, 2101-2127 (provided by Applicants) and further in view of Shalaby, et al. (US 6,221,958).

Kim teaches as set forth above. Kim does not explicitly teach that the composition is in the form of a cylindrical rod. Additionally, Kim does not teach that the hyaluronic acid ester is a cross-linked hyaluronic acid, the specific diameters and lengths of the cylindrical rod, forming and drying the osteogenic mxiture into a cylindrical rod, extruding the osteogenic mixture, whether in a nonsolvent (ethanol or water) or into the air, and drying.

Vercruysee discloses that sodium hyaluroate and hyaluronic acid are collectively determined as hyaluronan, abbreviated as HA. Pg. 514, first paragraph. Vercruysee additionally discloses that unmodified HA has found important applications in drug delivery and surgery and that the physiochemical properties of HA can be adapted to the desired application by chemical modification and furthermore it can be gathered that HA-drug hydrogels (would include HA

ester derivatives for drug delivery) may be used to localize a slow release formulation at a specific site in the body. Pp. 514-516. Vercruysee further discloses the production and possible used of chemically modified hyaluronic acids for drug delivery and in the Table shown on page 516 specifies derivatives of HA as, e.g. HA ester derivatives for the use in drug delivery and their availability from co-patentee Fidia (Advanced Biopolymers S.R.L.) and presents an overview of the in vitro and in vivo release studies performed with these material. Pp. 515-516, 528-534, 537-539. Vercuysee discloses on page 519 the esterification of the carboxylic acid groups of HA and in Table 2 on page 533 HYAFF11px (px referes to the percentage of carboxylic function modified) Hyaff11, which is one of the preferred compound of the instant application and used in the Examples is discussed as well as Hyaff11p50, and Hyaff11p75. Throughout the article.

Campoccia discloses hyaluronic Acid and partially or completely esterified forms of hyaluronic acid. See entire article, especially pg. 2103 (ester formation and the properties of the obtained hyaluronic acid ester are described). Campoccia discloses that cross-linking was a way to obtain a modified stable form of HA, that new classes of insoluble polymers were developed using a variety of cross-linking agents to trap HA chains within a net of cross-linked proteins or to create covalent bonds between HA chains and that the list of cross-linked derivatives is even longer and includes esterified HA chains. Pg. 2103. Additionally, Campoccia discloses that the vast majority of the described cross-linked materials are water insoluble gels with better viscosity and chemical stability that HA, and are generally susceptible to extensive hydration in aqueous solution. Pg. 2103. CAMPOCCIA DISCLOSES THAT Hyaff11 is one of the most characterized Hyaff polymers from both the physiochemical and biological view points and is

useful in understanding the effect that changing two variables, the type of ester and the percentage of esterification have on molecular properties, i.e. the extent of molecular modification modulates the soluble and viscous nature of the purified hyaluronan in aqueous solution and has proved to have profound effects on the inter action of hyaluronan with water (the higher percentage of esterification of hyaluronan, the lower its solubility in water; the total benzyl ester Hyaff11 sowed only slight hydration when placed in buffered phosphate saline solution and 75% hyaluronan benzyl esters, Hyaff1p75, hydration was even greater). Pg. 2103. Campoccia also discloses the degredation profiles between Hyaff11 (slower degredation, 2-3 months, more stable) and hydrated Hyaff11p75 (1-2 weeks) probably because partial esters are more flexible than more complete esterified ester in which the hydrophobic patches make the polymer chain network more rigid and stable. Pp. 2105 and 2112-2113. Campoccia further discloses that once esterification of the polymer has been obtained, the material can easily be processed to produce membranes, fibres, sponges, microsphes and other devices by extrusion, lyophilization or spray drying. Pg. 2103. Moreover Campoccia discloses the use of hyaluronan esters for drug delivery purposes or as a carrier. Pp. 2113-2114. Campoccia concludes that it is clear that hyaluronan derivatives have considerable potential as biomaterials because the may be prepared with varying degrees of stability, ranging from readily water-soluble to solid polymers with in vivo lifetimes measured in months and are cytocompatible polymer. Pp. 2120-2123.

Shalaby discloses sustained release formulations of proteins/peptides made from pastes and extruded from 18 gauge needles (close to 16 gauge and would have a diameter within 0.5 to 1.5 mm) to form rods and cut into lengths that had the proper dosage of drug and placed into a sterile 10 gauge needle (ready for injection). Cols. 4-5, lines 52-5, col. 6, lines 10- 17, col. 14,

lines 47-61, Example C-1 (col. 20), Example C-3 (col. 21), Example C-4 (col. 22), Claims 1, 5, 19, 20, 21, 28, 29, 30. Shalby does not explicitly discloses that the rods are dried. However, drying is implied as they are extruded and then loaded into a different gauge syringe and it would be difficult if not impossible to reload the rods without letting them harden.

Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to create a composition for injectable delivery of BMP-2 comprising BMP-2 and Hyaff11 (100% esterification) or Hyaff11p65 (65% esterification), wherein the composition is in the form of a cylindrical rod suitable for intraosseous injection in solid state into a body, where the diameter of the rod is between 0.5 and 1.5 mm with a reasonable expectation of success because the prior art suggests that HA benzyl ester derivatives are biodegradable, are intrinsically safe to use, can be used in sustained-release/drug delivery systems, can be extruded and are chosen based upon various physico-chemical properties, including viscosity, bioavailability, and degredation and that a preferred form of sustained release peptides in paste are extruded into rods and implanted and the matrix would not change the method. Additionally, the formation of rods through extrusion has the added benefits of being cheap and easily used decreasing the risks of implants that are associated with any type of surgery.

Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to create a composition for injectable delivery of BMP-2 comprising BMP-2 and Hyaff11 (100% esterification) or Hyaff11p65 (65% esterification), wherein the composition is in the form of a cylindrical rod suitable for intraosseous injection in solid state into a body, where the diameter of the rod is between 0.5 and 1.5 mm and the length is between about 2 cm to 5 cm with a reasonable expectation of success because the prior art suggests that HA benzyl ester

derivatives are biodegradable, are intrinsically safe to use, can be used in sustained-release/drug delivery systems, can be extruded and are chosen based upon various physico-chemical properties, including viscosity, bioavailability, and degredation and the length will be determined by comfort, needle length, dosage of the drug, all of which a skilled artisan would utilize in conjunction with the age of the patient, the severity of the illness, the weight of the patient, etc. to obtain optimal dosing and that a preferred form of sustained release peptides in paste are extruded into rods and implanted and the matrix would not change the method. Additionally, the formation of rods through extrusion has the added benefits of being cheap and easily used decreasing the risks of implants that are associated with any type of surgery.

Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to make a composition for treating osteoporotic bone comprising mixing BMP-2 and Hyaff11 or Hyaff11p65 to form an osteogenic mixture by hydration or solubilization of insoluble or partially soluble particles, films, fibers, non-woven pads, or sponges of Hyaff11 or Hyafflp65 in the presence of an organic solvent or aqueous buffer and forming by extrusion into the air and drying the mixture into a cylindrical rod suitable for intraosseous injection in solid state into a body with a reasonable expectation of success because the prior art suggests that HA benzyl ester derivatives are biodegradable, are intrinsically safe to use, can be used in sustained-release/drug delivery systems, can be extruded and are chosen based upon various physico-chemical properties, including viscosity, bioavailability, and degredation and that a preferred form of sustained release peptides in paste are extruded into rods and implanted and the matrix would not change the method. Additionally, the formation of rods through extrusion has the added benefits

of being cheap and easily used decreasing the risks of implants that are associated with any type of surgery.

Additionally it would have been obvious to one of ordinary skill in the art at the time of the invention to make a composition for treating osteoporotic bone comprising mixing BMP-2 and Hyaff11 or Hyaff11p65 to form an osteogenic mixture by hydration or solubilization of insoluble or partially soluble particles, films, fibers, non-woven pads, or sponges of Hyaff11 or Hyaffllp65 in the presence of an organic solvent or aqueous buffer and forming by extrusion into a nonsolvent, such as water or ethanol, and drying the mixture into a cylindrical rod suitable for intraosseous injection in solid state into a body with a reasonable expectation of success because the prior art suggests that HA benzyl ester derivatives are biodegradable, are intrinsically safe to use, can be used in sustained-release/drug delivery systems, can be extruded and are chosen based upon various physico-chemical properties, including viscosity, bioavailability, and degredation; that a preferred form of sustained release peptides in paste are extruded into rods and implanted and the matrix would not change the method; and that extruding the mixture into a nonsolvent would permit the extrusion to remove any impurities that are soluble and/or would ease the flow of the paste through the syringe. Additionally, the formation of rods through extrusion has the added benefits of being cheap and easily used decreasing the risks of implants that are associated with any type of surgery.

Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to create a composition for injectable delivery of BMP-2 comprising BMP-2 and Hyaff11 (100% esterification/crosslinked) or Hyaff11p65 (65% esterification/crosslinked), wherein the composition is in the form of a cylindrical rod suitable for intraosseous injection in

solid state into a body, where the diameter of the rod is between 0.5 and 1.5 mm and the length is between about 2 cm to 5 cm with a reasonable expectation of success because the prior art suggests that HA benzyl ester derivatives are biodegradable, are intrinsically safe to use, can be used in sustained-release/drug delivery systems, can be extruded and are chosen based upon various physico-chemical properties, including viscosity, bioavailability, and degredation and the length will be determined by comfort, needle length, dosage of the drug, all of which a skilled artisan would utilize in conjunction with the age of the patient, the severity of the illness, the weight of the patient, etc. to obtain optimal dosing; that a preferred form of sustained release peptides in paste are extruded into rods and implanted and the matrix would not change the method and to improve the stability of the HA and HA derivatives and would exclude the leaching of any toxic cross-linking agents which may be used to bridge polymer chains as taught by Campoccia and thus improve the stability and safety of the matrix. Additionally, the formation of rods through extrusion has the added benefits of being cheap and easily used decreasing the risks of implants that are associated with any type of surgery.

12. Claims 81-83 and 101-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim, et al., (WO 01/28602 A1) in view of Vercruysee, et al., Hyaluronate Derivatives in Drug Delivery, Critical Review in Therapeutic Drug Carrier Systems, 1998, 15(5), 513-555 and Campoccia, et al., Semisytnetic resorbable materials from hyaluronan esterification, Biomaterials, 1998, 19, 2101-2127 and further in view of Shalaby, et al. (US 6,221,958 and further in view of Daifotis, et al. (US 6,015,801).

Kim, Vercruysee, Campoccia and Shalby disclose as set forth above. However, none of them disclose the addition of alendronate, a biphosphonate compound for inhibiting bone

resorption in patients with osteoporosis. See, e.g., Daifotis, col. 1, lines 55-60. Daifotis discloses that despite their therapeutic benefits, biphosphonates (which would include alendronate) are poorly absorbed from the gastrointestinal tract and that intravenous administration has been used to overcome this bioavailability problem but that i.v. administration is costly and inconvenient, especially when the patient must be given an intravenous infusion lasting several hours on repeated occasions. Col. 2, lines 4-16. Daifotis also discloses that when oral administration of the bisophosphonate is desired relatively high does must be administered to compensate for the low bioavailability from the gastrointestinal tract and that oral administration has been associated with adverse gastrointestinal effects, especially those relating to the esophagus.

Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to have added alendronate to the BMP-2/Hyaff11 or Hyaff11p65 matrix with a reasonable expectation of success because the prior art suggests that other drugs can be added to the matrix without any adverse effects, that the composition is useful to treat osteoporosis fractures, that alendronate will be utilized if it reaches the blood stream and that if alendronate is included in the matrix, the problems associated with oral and intraveneous methods of administration will be alleviated, i.e. one would have increased availability of the drug, lower costs, better compliance and increase convenience.

Double Patenting

13. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v.*

Eagle Mfg. Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

14. Claims 72, 74, 85, 92, 99, 105, 107, 113, and 116 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 3, 9, 11, 14, 15,17, 19, and 25-27 of prior U.S. Patent No. 7,189,392. The U.S. Patent discloses in the Summary of the Invention that "[t]he methods and compositions of the present invention are useful for the preparation of formulations of osteoinductive proteins …, "the injectable formulations of the invention allows for closed fracture repair and other skeletal tissue without an open reduction procedure…" and "… provides injectable formulations". Thus injectable through the skin would encompass intraosseous injection and would implicitly be a cylindrical rod because when pastes/gels are injected through a needle for intraosseous injections, or otherwise, the material coming out of the needle is in the form of a solid rod because it is being extruded, in a similar fashion to the instant application's extrusion from a needle. This is a double patenting rejection.

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 72, 74, 85, 92, 99, 105, 107, 113, and 116 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 9, 11, 14, 15,17, 19, and 25-27 of U.S. Patent No. 7,189,392 in view of Shalaby, et al. (US 6,221,958). Shalaby discloses sustained release formulations of proteins/peptides made from pastes and extruded from 18 gauge needles (close to 16 gauge and would have a diameter within 0.5 to 1.5 mm) to form rods and cut into lengths that had the proper dosage of drug and placed into a sterile 10 gauge needle (ready for injection). Cols. 4-5, lines 52-5, col. 6, lines 10- 17, col. 14, lines 47-61, Example C-1 (col. 20), Example C-3 (col. 21), Example C-4 (col. 22), Claims 1, 5, 19, 20, 21, 28, 29, 30. Shalby does not explicitly discloses that the rods are dried. However, drying is implied as they are extruded and then loaded into a different gauge syringe and it would be difficult if not impossible to reload the rods without letting them harden. Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to have utilized the procedure in Shalby because it provides a cheap and efficient way to produce the sustained release compositions of the invention with a reasonable expectation of success.

Conclusion

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Rueger, et al., Matrix-Free Osteogenic Devices, Implants and Methods of Use

Thereof, US 6,281,195 B1, August 28, 2001, discloses the injectable formulations of osteogenic proteins (including BMPs) admixed with a carrier, which is a sugar (noting that HA is a sugar).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer I. Harle whose telephone number is (571) 272-2763. The examiner can normally be reached on Monday through Thursday, 6:30 am to 5:00 pm,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer I. Harle
Examiner
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